

Application No. 10/521,930

Reply to Office Action

*REMARKS/ARGUMENTS**The Pending Claims*

Claims 1-13, 15, and 17-19 are pending. Claims 1-9 (and 10) are currently being examined, whereas claims 11-13, 15, and 17-19 are withdrawn.

Notice of Non-Compliant Amendment

A "Reply to Office Action" was originally filed May 19, 2006 in good faith, but pages 8-14 of the Reply were inadvertently not transmitted. Applicants submit herewith the full text of the Reply to Office Action filed May 19, 2006 but retitled as "Reply to Notice of Non-Compliant Amendment."

Amendments to the Claims

Claim 1 has been amended to delete the phrase "or prodrug." Claim 10 has been amended to delete non-elected subject matter. Claims 14, 16, and 20-22 have been canceled as directed to non-elected subject matter, and claims 11-13, 15, and 17-19 have been withdrawn. No new matter has been added by way of these amendments.

Summary of the Office Action

The Office maintains the restriction requirement. Claim 1 was rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claim 1 was rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description. Claims 1-9 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. Reconsideration of the pending claims is hereby requested.

Discussion of the Restriction Requirement

The Office maintains the restriction requirement between Groups I-IV. Claims 14, 16, and 20-22 have been canceled as directed to non-elected subject matter. In addition, claim 10 of Group II has been amended to delete non-elected subject matter and to be commensurate in scope with claim 1. Applicants respectfully request that amended claim 10 be examined with claims 1-9 of Group I.

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The method claims of Group III (i.e., claims 11-13, 15, and 17-19) have been withdrawn from consideration but the Office has indicated that such claims may be rejoined for examination if the subject matter of Group I is found allowable and the withdrawn claims are amended to be commensurate in scope with the allowed subject matter.

Discussion of the Indefiniteness and Written Description Rejection of Claim 1

Claim 1 has been rejected as allegedly indefinite and lacking written description because of the term "prodrug." This term has been deleted from claim 1, and as a result, these rejections of claim 1 are moot.

Discussion of the Enablement Rejection

Applicants traverse the non-enablement rejection. Example 1 of the specification describes the solution and purification of poecillastrin A from frozen Poecillastrin sponge. Samples of the sponge Poecillastrin species were collected at a depth of -359 meters near Settlement Point, Grand Bahamas Island, Bahamas, and a voucher of specimen (#Q66B974) for this collection is maintained at the Smithsonian Institution, Washington, D.C. Based on this detailed disclosure as the source of the sponge and method for isolation of, there is no doubt that the specification enables the isolated and purified poecillastrin A.

The specification then describes how to make the compounds by chemically modifying various oxygen- and nitrogen-containing groups in order to synthesize the compounds of the claims. For example, the specification describes suitable substituents for the compound of formula (I), including detailed descriptions of the various organic moieties (e.g., page 7, line 16, to page 12, line 13). Synthetic methods of preparing compounds of formula (I) by direct methods or modification of poecillastrin A are described at, for example, page 12, line 14, to page 13, line 31. For example, the specification describes how a hydroxyl group can be converted to an ester with an esterifying agent, such as an anhydride or acid chloride (page 12, lines 26-28). The specification explains that in addition to the methods described therein, the compounds of formula (I) can be prepared using routine chemistry that is well known in the art (see, for example, page 13, lines 27-29). The specification also describes the isolation and purification of certain compounds of the present invention, when obtained as solvent extracts from marine sponges (page 29, line 31, to page

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31, line 27). Definitive proofs of the structure of the isolated compounds can be determined based on the methods described at, for example, page 31, lines 28-32.

The specification also teaches one of ordinary skill in the art how to use the invention. In particular, methods for determining the vacuolar-type (H⁺)-ATPase inhibitory activity and cytotoxicity for compounds of formula (I) are described in the specification at, for example, page 19, line 6, to page 29, line 30. For example, the NCI 60 cell-line screen identifies the degree of growth inhibition and/or cytotoxicity of compounds that are tested over a defined range of concentrations against a panel of 60 different human tumor cell lines. For each compound tested, both the absolute and relative sensitivities of individual cell lines comprising the screen provide a characteristic profile or "fingerprint" of the compound's activity. Using COMPARE (computerized, pattern-recognition algorithm), novel compounds with screening "fingerprints" matching standard agent(s) having known or presumed known mechanism(s) of action can be identified. Specifically, exemplary compounds of formula (I) were found to have characteristic screening "fingerprints" that correlate with prototypical vacuolar-type (H⁺)-ATPase inhibitory compounds: concanamycin A, bafilomycin A1, salicylhaliamide A, and lobatamide A, all of which are structurally unrelated to compounds of the invention (page 27, lines 8-25). Thus, the NCI 60 cell-line screen is useful for demonstrating that a compound of the present invention is an inhibitor of vacuolar-type (H⁺)-ATPase. In addition, Example 3 illustrates the general procedure for obtaining the activity profile of exemplary compounds of the invention using the NCI 60 cell-line screen. Examples 4-6 illustrate the vacuolar-type (H⁺)-ATPase inhibitory activity and cytotoxicity of compounds of the invention (e.g., an extract of *Poecillastra* species and poecillastrin A).

Furthermore, exemplary conditions that are susceptible to prevention or treatment by a compound of formula (I) are described in the specification at, for example, page 16, line 27, to page 18, line 7. Formulations of compounds of formula (I) are described in the specification at, for example, page 14, line 4, to page 16, line 13 and page 18, lines 18, to page 19, line 5, and includes modes of administration, carriers, and concentrations. Suitable doses are described in the specification at, for example, page 16, lines 14-26.

Therefore, in view of the foregoing, one of ordinary skill in the art would be able to make and use the compounds of the present invention, without undue experimentation.

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Accordingly, claims 1-10 are enabled by the specification, and this rejection should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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